

5-7 JUNE 2018 OSLO, NORWAY

# Report on Radioisotope Production By Working Group 3 Chaired by the Netherlands

version after discussion in Oslo

# 1. Summary

This paper is one of three discussion papers for the June 2018 Oslo Symposium Meeting. The other two papers discuss: the conversion of research reactors from HEU to LEU fuel; and the removal and disposition of un-needed HEU inventories. This paper discusses progress made to minimize the usage of HEU in radioisotope production, and how to address the remaining producers of Mo-99 that rely on HEU targets. It also notes the progress of medical radioisotope producing reactors that still require HEU fuel in converting to the use of LEU fuel.

The following sections discuss: an inventory of the major producers of medical radioisotopes on the global market, HEU/LEU usage and conversion commitments, technological advances, financial aspects of production, fundamental principles for market regulation, and a summary and potential discussion points for the Symposium.

# 2. Stocktake of current and near future producers of medical radioisotopes

The major global suppliers of medical radioisotopes are located in Australia, Belgium, The Netherlands, and South Africa (comprising over 90% of the world market). Currently, other producers are suppliers on their domestic market and hold a small share in the global market (e.g. suppliers in Russia). New initiatives for the production of medical radioisotopes are noted in Argentina, Egypt, France, Germany, India, Italy, Kazakhstan, Korea and the United States. Some of these countries, notably United States, Canada and Italy, consider alternative non-fission based production technologies.

The table below indicates the fuel and targets used and/or planned to be used by producers of Mo-99. Australia (ANSTO) has produced Mo-99 from LEU targets for many years. South Africa (NECSA) and The Netherlands (Curium Pharma), with technical and financial support from the United States, converted their Mo-99 production processes from HEU to LEU targets in August 2017 and January 2018, respectively. Belgium (IRE) is in the process of converting their targets, and plans to complete its conversion by 2020.

Existing Irradiators	Reactor Fuel	Targets	Reactor	Processor	Production Capacity (6-day Ci/week)
Argentina	LEU (per 1989)	LEU (per 2002)	RA-3 (Ezeiza)	CNEA	400
Australia	LEU (from 2005)	LEU (from start)	OPAL (Sydney)	ANSTO	2,150
Belgium	HEU (to 2026)	HEU (some more years) LEU (per 2018)	BR2 (Mol)	IRE (Fleurus) Curium Pharma (Petten, NL)	7,800
Canada	HEU (stop March 2018)	no future production (?) (accelerators?)	NRU (Chalk River)	MDS-NORDION (Kanata)	0
Czech Republic	LEU (per 2011)	HEU (LEU ready, at request IRE)	LVR-15 (Rež)	IRE (Fleurus, Belgium)	3,000
The Netherlands	LEU (per 2006)	LEU (per 2018) HEU (some more years)	HFR (Petten)	Curium Pharma (Petten) IRE (Fleurus, Belgium)	6,200
Poland	LEU (per 2014)	LEU (per 2018)	MARIA	Curium Pharma (Petten, NL)	2,200
Russia	HEU	HEU	RIAR and IPC		
South Africa	LEU (per 2009)	LEU (per August 2017)	SAFARI-1 (Pelindaba)	NECSA (Pelindaba)	3,000
New	Reactor Fuel	Targets	Reactor	Processor	Start Date
Irradiators	LEU	LEU		CNEA	and Production Capacity (if known)
Argentina	LEU	LEU	RA-10 (Ezeiza)	CNEA	After 2020 (2500 6dCi/week)
Egypt	LEU	LEU	ETRR-2	AEA (Egypt Atomic Energy Authority)	
France	HEU	LEU	Jules Horowitz Reactor – JHR - (under construction)	CEA	2022
Germany	HEU	LEU	FRM II	IRE (Fleurus) Curium Pharma (Petten, NL)	2019
India	LEU	LEU	Dhruva (Mumbai)	BRIT	
Italy	LEU	Mo-98 targets	TRIGA-RC 1	unknown	2020
			(actually in operation)		30-100 Ci/week
Kazakhstan	LEU	Mo natural targets	WWR-K (Alatau)	NTI (Inst. of Nucl. Physics)	50 Ci
Korea	LEU	LEU	KJRR	KAERI	2023 (400 Ci/week → 2000 Ci/week)
The Netherlands	LEU	LEU	PALLAS	Curium Pharma (Petten, NL) IRE (Fleurus, Belgium)	2025
United States	HEU	Mo-98 targets	MURR (commencing in 2018)		



3. Status of HEU/LEU usage and conversion commitments by current and future producers

The working group has identified the following commitments that have been fulfilled by the following nations.

#### Australia

Australia has a strong commitment to minimising the use of HEU in Mo-99 production. Australia's new multi-purpose, research reactor OPAL which was commissioned in 2006, was conceived and designed to run on LEU fuel. In 2004-06, Australia converted HIFAR, its previous research reactor (now closed-down and awaiting decommissioning), to LEU fuel. Since Australia began Mo-99 production in the early 1970's, Australia has always used LEU targets.

#### Czech Republic

The Czech Republic has strong commitment to minimising the use of HEU. The LVR-15 reactor fuel was successfully converted to LEU in 2011 and the reactor has completed the qualification process for irradiation of LEU targets in September 2015. Since then, both HEU and LEU targets are irradiated regularly. The Mo-99 production will be fully converted to LEU on foreign customer's request as soon as the LEU processing line is ready for commercial operation, which is expected before the end of 2018.

# Italy

#### Moly Project at TRIGA RC1

During the last two years, a theoretical-experimental activity has been carried out on the activation of Mo-98 in research reactors, the outcomes demonstrate that such technology is really promising and available in the short term. The Molybdenum Project aims to the intensive use of the research reactor TRIGA RC-1 (Training Research Isotopes General Atomics - Reactor Casaccia 1) of the ENEA Casaccia Research Center for the production of Mo-99. The nuclear research reactor TRIGA RC-1 is a source of thermal neutrons with LEU fuel; it was built in 1960 in its first version with 100 kW of power under the USA Atoms for Peace initiative and subsequently, in 1967, it was brought to the power of 1 MW by ENEA.

Based on the neutron characteristics of the reactor, and taking into account recent studies related to similar plants, a theoretical evaluation of the potential production has been carried out assuming the irradiation of a target of metallic molybdenum enriched to 98.4% in Mo-98 in the central channel of the core. The theoretical evaluation, confirmed by experimental measurements of irradiated targets of natural Molybdenum, give a range of production from 30 to 100 Ci/week, depending on the irradiation mode (continuous or discontinuous).

**NSFS** 



The production of Mo-99 can also be done with the use of fast neutrons, in particular those generated by the nuclear fusion of deuterium and tritium. This production is based on the use of targets enriched in Mo-100 but is in fact inaccessible because there is no source in the world with a sufficiently intense 14 MeV neutron flux.

A feasibility study on this alternative route to reactors to produce Mo-99 from fast fusion neutrons was conducted in ENEA and the experimental findings, supported by Monte Carlo calculations, were very promising.

The success of these experimental tests led ENEA to consider the idea of creating an intense neutron source, called the New Sorgentina Fusion Source (NSFS), which could generate a 14 MeV neutron flux suitable for the industrial production of Mo-99 (around or higher than 1000 Ci/week).

#### Kazakhstan

For the production of Mo-99 and Mo-99 / Tc-99m generators Kazakhstan uses molybdenum oxide of natural isotope composition as a target for irradiation at the WWR-K reactor. Production has been carried out since 2001 in the volume of 10 Ci 2 times a month. The potential for production of 6-day  $(n, \gamma)$  Mo-99 is 50 Ci / week.

### Republic of Korea

The Republic of Korea shall contribute to the development of a high density LEU target and UMo fuel to promote the use of LEU for the production of medical purpose radioisotopes.

### The Netherlands

Dutch commitments in NSS have been fulfilled, and future processing of (LEU) targets will be in line with the commitments.

The Netherlands has completed both the fuel and the target conversion in the current HFR (Petten) and Curium Pharma (Petten).

A tender for a new reactor (PALLAS), designed to use both LEU fuel and LEU targets, has been won by an Argentine-Dutch combination.

### **Poland**

Maria research reactor was fully converted from HEU to LEU fuel in August 2014. From January 2018 only LEU targets are irradiated under the agreement with Curium Pharma (Petten, The Netherlands).

#### **USA**

The United States leads global HEU minimization efforts in Mo-99 production by cooperating with the major global Mo-99 producers in converting their production processes from HEU to LEU fuel and targets, and by supporting the establishment of reliable, commercial, non-HEU-based Mo-99 production in the United States. The United States provided financial and technical support for Mo-99 conversions in South Africa and The Netherlands, and continues to provide similar support to Belgium in its ongoing conversion effort. The United States has also provided up to \$25 million to accelerate four non-HEU-based Mo-99 production projects in the United States. The first of these four technologies, NorthStar Medical Radioisotopes' neutron capture project, will begin producing Mo-99 for patient use in 2018.



# 4. Pursuit of technological advances to minimise the use of HEU in Mo-99 production

Technological effort aimed at minimising the use of HEU in Mo-99 production can be broken into three main areas: the development of alternative technologies (e.g. neutron capture technologies and accelerator-based technologies); the development of high performance LEU fuels; and the development of high-density LEU targets. Work in all these areas has been ongoing for decades.

The first non-uranium-based technology to produce Mo-99 on a commercial scale will be a neutron capture technology in the United States; Mo-98 targets will be irradiated in the Missouri University Research Reactor (MURR). MURR is currently HEU-fuelled but scheduled for conversion by 2028 if suitable LEU fuel becomes available.

The accelerator technologies currently being investigated for the production of Mo-99 or Tc-99m are:

- Production of Mo-99 with linear accelerators using enriched Mo-100 targets
- Direct production of Tc-99m with cyclotrons using enriched Mo-100 targets
- Fission of LEU targets using neutrons produced by accelerators

Work on these production methods is ongoing in the US, Canada, and other nations.

While current LEU target technology is able to produce large volumes of high-quality Mo-99, work will continue to develop higher-density LEU targets that produce Mo-99 more efficiently than current LEU target technology.

### 5. Financial aspects of the production of medical radio isotopes

# a. HEU and LEU and the costs and efficiency of producing Mo-99

It is recognized by all that HEU minimization in Mo-99 production must be undertaken in a way that ensures a continued reliable supply of Mo-99 for patient use. There are a number of financial disincentives in converting Mo-99 production from HEU to LEU targets. The yields of Mo-99 from HEU targets are higher than those from LEU targets; and production of Mo-99 from LEU targets produces (up to four times) bigger volumes of waste than Mo-99 production from HEU targets. Therefore, it is cheaper to produce Mo-99 from HEU targets than from LEU targets.

### b. Research reactors with HEU as a fuel

Some reactors that produce Mo-99 still require HEU fuel to fulfil their diverse missions, one of which may be Mo-99 production. The BR-2 reactor in Belgium and the MURR in the United States are working to convert to high-density LEU fuels currently under development as soon as technically and economically possible. The FRM-II reactor in Germany uses HEU fuel, intends to produce Mo-99 from LEU targets from 2019 and to convert to using high density LEU fuels as soon as it is available The Jules Horowitz reactor in Cadarache, France, will initially use HEU as a reactor fuel but intends to convert to high-density LEU fuel once it is available.



Several countries, most notably Australia, France (from 1997 to 2015), Germany (from 2002 to 2006), The Netherlands and South Africa, are producing Mo-99 from LEU fueled reactors.

### c. Price consequences of conversion

It is recognized that LEU conversion increases the costs of Mo-99 production. It is also recognized that a sustainable and reliable global Mo-99 market requires that these increased costs be built into the economic model of the Mo-99 supply chain. The international Mo-99 community, via industry, governments, and the OECD HLG, continues to work to reflect the true cost of Mo-99 product in pricing but recognizes that estimating the (true) cost of Mo-99 production in research and test reactors is a major challenge, as there are so many missions for these reactors. This of course influences ensuring a sustainable and reliable Mo-99 industry.

# 6. Fundamental principles for market regulation

In 2011, the OECD/NEA formulated – through the High-level Group on the Security of Supply of Medical Radioisotopes (HLG-MR) – six principles regarding policy actions necessary to ensure the long-term security of supply of medical radioisotopes (www.oecd-nea.org/med-radio/statement). These principles have formed the basis for the international community's activities to support a sustainable and reliable Mo-99 market for the future. This Symposium supports additional efforts by governments to augment and strengthen the current work being done in furtherance of these principles.

### OECD/NEA principles

- Principle 1. All Tc-99m supply chain participants should implement full-cost recovery, including costs related to capital replacement.
- Principle 2. Reserve capacity should be sourced and paid for by the supply chain. A common approach should be used to determine the amount of reserve capacity required and the price of reserve capacity options.
- Principle 3. Recognising and encouraging the role of the market, governments should:
  - establish the proper environment for infrastructure investment;
  - set the rules and establish the regulatory environment for safe and efficient market operation;
  - ensure that all market-ready technologies implement full-cost recovery methodology; and
  - refrain from direct intervention in day-to-day market operations as such intervention may hinder long-term security of supply.
- Principle 4. Given their political commitments to non-proliferation and nuclear security, governments should provide support, as appropriate, to reactors and processors to facilitate the conversion of their facilities to low enriched uranium or to transition away from the use of highly enriched uranium, wherever technically and economically feasible.
- Principle 5. International collaboration should be continued through a policy and information sharing forum, recognizing the importance of a globally consistent approach to addressing security of supply of Mo-99/Tc-99m and the value of international consensus in encouraging domestic action.



Principle 6. There is a need for periodic review of the supply chain to verify whether Mo-99/Tc-99m producers are implementing full-cost recovery and whether essential players are implementing the other approaches agreed by the HLG-MR, and that the co-ordination of operating schedules or other operational activities have no negative effects on market operations.

To augment these OECD principles, countries should take the following actions to ensure a sustainable and reliable Mo-99 industry:

- Complete the conversion of all major Mo-99 producers from HEU to LEU targets;
- Continue to support the development of new non-HEU-based technologies to ensure a technically diverse Mo-99 production base that is not reliant upon a single technology;
- Support OECD HLG efforts to engage government health ministries on the issue of appropriate reimbursement of non-HEU-based Mo-99 procedures.
- Strongly discourage the procurement of Mo-99 produced from HEU targets and encourage the procurement of Mo-99 produced without HEU. Continue to support ongoing efforts to convert HEU-fuelled research reactors to LEU fuel.
- Consider the proliferation effects of supplying HEU fuel to new market entrants.

# 7. Summary and potential discussion points for June Symposium

- The ideal medical radioisotope production would not use HEU. In principle, the technical challenges involved in conversion of HEU based production to LEU based production can be overcome, as has been demonstrated in practice. However, also market challenges exist.
- The question whether reactors producing medical isotopes using HEU-fuel disincentivises HEU minimisation efforts. An inventory of the progress vis-a-vis the use of LEU fuel and targets is presented in the table on page 2. The technical aspects of conversion of fuel from HEU to LEU are addressed in WG 1.
- The most widely used medical radioisotope, Molybdenum-99 (Mo-99) is predominantly made by irradiating uranium bearing targets in research and test reactors.
- The Mo-99 supply chain remains fragile, and all countries place top priority on maintaining a secure, stable Mo-99 supply for patient use.
- Currently only a few countries/companies service the Mo-99 world market. All of the current major global Mo-99 suppliers either use LEU targets, or aim at producing with LEU targets by 2020.
- Some producers still use HEU targets. After 2020 only smaller-scale producers will use HEU targets.



- It has been technically and commercially demonstrated that it is possible to make Mo-99 from LEU targets and via neutron capture by Mo-98 targets.
- Mo-99 can be produced using accelerators (e.g. via electron irradiation of Mo-100). However such methods have not been proven on a commercial scale and have not yet gained regulatory approval.
- Whilst Mo-99 represents the overwhelming majority of medical radioisotope production, there are other isotopes which are commonly used and produced in reactors by fission of U-235 (e.g. I-131, Xe-133).

#### Nations should consider:

- How to begin or continue developing new non-HEU-based technologies to ensure a technically diverse Mo-99 production base that is not reliant upon a single technology.
- How to support OECD HLG efforts to engage government health ministries on the issue of appropriate reimbursement of Mo-procedures; reimbursement is an important aspect in addressing the issue of the increased costs of non-HEU-target based production.
- How to support current producers in completing their conversions from HEU to LEU targets, and how to support ongoing efforts to convert HEU-fuelled research reactors to LEU fuel.
- How to ensure that no new producers that use HEU targets are allowed to enter the market.
- How to further minimize the use of HEU, where technically and economically feasible, through the conversion of reactor fuel from HEU to LEU and the development and qualification of LEU fuels for high performance research reactors (as consistent with Working Group 1).
- How to further develop, promote and use non-HEU-based technologies for the production of medical radioisotopes.

